SEPTICAEMIA IN A GENERAL HOSPITAL

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Since the introduction of antibiotics, there has undoubtedly been a reduction in the incidence of septicaemia, but the likelihood that a direct attack on the invading organism would greatly reduce the morbidity and mortality of established septicaemia has not been confirmed in practice.

Spink (1954), reviewing the deathrate for cases of staphylococcal septicaemia and osteomyelitis treated in the University of Minnesota Clinic, gives a mortality of over 80 per cent. for those seen between 1933 and 1941. After the introduction of penicillin, the rate fell, being 28 per cent. from 1942 to 1944, but rose to 54 per cent. from 1951 to 1953, although additional antibiotics were available by then. Recently (Spink, 1956), the deathrate for the period 1952 to 1955 for cases of staphylococcal septicaemia and endocarditis is given as 80.5 per cent., a figure similar to that for the pre-antibiotic period. Similar figures are given by Mendell et al. (1939) for the mortality in staphylococcal septicaemia before the introduction of antibiotics. Dowling et al. (1952) considering 25 cases of staphylococcal endocarditis and 76 collected from the literature found a deathrate of 48 per cent. in their personal series and 53 per cent. in the collected series.

Spittel et al. (1956) discussed the problem of septicaemia due to Gram negative organisms, describing 137 cases seen during 15 years. They quote previous mortality figures for B. coli septicaemia of 40 per cent. (Jacob, 1909); 35.7 per cent. in the pre-sulphonamide and 21.4 per cent. in the post-sulphonamide period (Herrell and Brown, 1941); and 23.5 per cent. in streptomycin-treated cases (Committee on Chemotherapeutics, 1946). In their own series, there was a mortality of 25 per cent. of 76 cases of B. coli septicaemia. The number of cases of septicaemia due to other organisms was smaller, but the trend was towards a lower deathrate e.g. B. proteus infection had a mortality of 64 per cent. in one series (Abrams, 1948) and of 27 per cent. in the series of Spittel et al. The problem of antibiotic resistance is not so great with Gram negative organisms as it is with staphylococci.

The cases described below comprise all those with a positive blood culture and evidence of severe infection admitted to the general medical, general surgical and trauma wards of the General Hospital, Birmingham, between October 1, 1955, and March 31, 1957. There are 24 cases in the group. A few cases were seen, in whom clinical or post-mortem evidence of septicaemia was present, but a positive blood culture was not obtained. These have been excluded. Cases of subacute bacterial endocarditis have not been considered. The total number of admissions to the wards concerned during the period under review was 10,004 (medical 3,722, surgical 3,454 and trauma 2,828).

Routine antibiotic sensitivity tests were performed using tablets impregnated with antibiotics in the following concentrations per tablet: penicillin, 2.5 units; chloramphenicol, 100 μg.; tetracycline, 100 μg.; streptomycin, 80 μg.; erythromycin, 10 μg. The organism to be tested was subcultured on to a blood agar plate and the zone of inhibition observed around the different tablets. In special cases, the sensitivity was determined using tubes containing varying concentrations of antibiotics.

Description of Cases

In this series of 24 cases, there were 11 cases of staphylococcal infection, with eight deaths and 13 cases of non-staphylococcal infection, with four deaths.

Staphylococcal Infections

Staphylococcal infection has been the greatest problem, accounting for seven of the 11 deaths which occurred during the acute illness and for the one late death. Of the 12 surviving cases, only three had staphylococcal infections. In three
patients the strain of staphylococcus isolated was sensitive to all antibiotics tested, but in spite of apparently adequate treatment, all three died.

Case 1 had originally been investigated to find the cause of diarrhoea which had been present for a year. The only abnormal finding had been a Staph. aureus in the faeces. This organism was resistant to penicillin and sensitive to other antibiotics, and the diarrhoea had ceased after treatment with tetracycline. Later, acute retention of urine developed due to a prostatic abscess, which was drained. Unfortunately, at this stage, penicillin was given, though the organism originally isolated was known to have been resistant to this antibiotic. Steady deterioration followed the operation, with high fever, pulmonary embolism, and finally the signs of a metastatic abscess in the cervical spine. Death occurred in a state of shock five days after a positive blood culture was obtained and in spite of treatment with all available antibiotics. The organism at this stage was slightly sensitive only to streptomycin and erythromycin.

At autopsy chronic prostatic abscesses were found which were probably the source of the original infection and the cause of the diarrhoea. This appears to be a case in which there was an increase in resistance to antibiotics of an organism which was originally only penicillin resistant, though it is possible that the organism isolated later was acquired in hospital.

Case 2 had had chronic osteomyelitis of the right elbow following a gun-shot wound received in the 1914-18 war. A discharging sinus developed in 1947. This was incised in December 1957, and three days later, gross cellulitis was present with signs of axillary vein thrombosis. A swab from the wound and a blood culture yielded a Staph. aureus fully sensitive to antibiotics. In spite of treatment, progressive respiratory and cardiac failure occurred and autopsy showed multiple lung abscesses.

In case 3, there had been an acute illness for five days before admission to hospital, at which time, purpuric patches were observed on the extremities. A few hours afterwards, signs of hemiplegia due to cerebral embolism appeared and three days later, there was the onset of complete heart block followed by cardiac failure. At autopsy, acute bacterial endocarditis was present and there was a small interventricular septal defect, presumably acquired, at the site of the bundle of His.

Case 4 had been ill for three weeks before admission to hospital. A diagnosis of septicaemia was made, but no focus of infection could be found at this time. After seven days, peritonitis developed and a gangrenous appendix was removed. Numerous liver abscesses were seen at operation. The infection was never completely controlled, and at autopsy multiple liver abscesses and an encysted empyema were seen.

Case 5 is an example of a fulminating infection with a resistant organism which was acquired after prostatectomy in a previously healthy man. Ascending pyelonephritis led to death from renal failure.

Case 6 was a young woman already seriously ill with tuberculous polyserositis and meningitis. Diarrhoea developed and a Staph. aureus sensitive to chloramphenicol and erythromycin was isolated from the faeces. She became jaundiced and increasingly febrile. Blood cultures were performed and a Staph. aureus, sensitive only to chloramphenicol and erythromycin, and a B. coli were isolated. Death occurred in coma, presumably due to liver failure. At autopsy no metastatic abscesses were found. The diagnosis of tuberculosis was confirmed by guinea-pig inoculation with ascitic fluid. The staphylococcal infection was acquired in hospital. The part it played in causing death is difficult to estimate, but there was no autopsy evidence of active infection. The cause of the liver failure is unknown.

Case 7 had had chronic osteomyelitis affecting many bones since 1916 and had extensive amyloid disease. He developed fever, and a Staph. aureus, sensitive to all antibiotics except tetracycline, was isolated on blood culture. On admission, his blood urea was 57 mg., and this rose to 315 mg. two days before death. No abscesses were found at autopsy. It is assumed that the septicaemia was a terminal infection in a case of progressive renal failure due to extensive infiltration of the kidneys with amyloid, which was demonstrated histologically.

Case 12 had chronic rheumatic heart disease. He presented with multiple emboli and fever. Blood culture grew a Staph. aureus, fully sensitive to antibiotics. The infection was controlled, but he developed progressive congestive cardiac failure and died at home nine months later.

Case 13 had had a foreign body in the cheek following a road accident 15 years ago. Since then there had been an intermittently discharging sinus in the neck, which may have been the source of infection. A Staph. aureus partly sensitive to streptomycin, chloramphenicol, tetracyclines and erythromycin was isolated on blood culture.

Case 14 was seriously ill on admission with peritonitis secondary to appendicitis. Blood culture, not performed until after a second operation for drainage of a pelvic abscess yielded a Staph. aureus partially sensitive to all antibiotics tested.

Case 15 was suffering from diabetic ketosis and
pneumonia. High fever persisted in spite of treatment with penicillin, tetracycline, chloramphenicol and streptomycin. Three weeks after admission, a Staph. aureus sensitive only to erythromycin and chloramphenicol was found in the blood and also on culture of a vaginal swab. Six weeks after admission, an abscess of the buttock was incised and the patient became afebrile.

Non-Staphylococcal Infections

There are 13 cases of non-staphylococcal infection in this series, with four deaths. Two (Cases 10 and 11) occurred terminally in patients suffering from malignant disease, one of whom also had subacute nephritis causing the nephrotic syndrome. In these cases the signs of an acute infection appeared eight and 19 days before death, and the bacteremia was not a terminal finding. The remaining two deaths were both in patients with severe liver disease. Case 8 was a Pakistani probably suffering from kala-azar though Leishmania donovani was not seen in histological sections of the spleen. Liver function tests were abnormal (Table 2) and the formol gel test was positive. The original pneumococcal blood-stream infection, associated with pneumonia and meningitis was controlled by penicillin treatment. Unfortunately, following urethral catheterisation, infection with B. pyocyanus occurred leading to a second episode of septicaemia and death from uraemia due to acute pyelonephritis. Case 9 was a West African who had had obstructive jaundice for nine months, and had grossly abnormal liver function tests (Table 2). Partial pancreatectomy was performed for removal of a carcinoma of the ampulla of Vater. Six weeks post-operatively meningitis and septicaemia due to B. friedlander developed, death occurring in coma after eight days. At autopsy, purulent meningitis and multiple liver abscesses were present. The anastomosis was patent and there was no sign of recurrence of carcinoma.

There were nine survivors in the group of non-staphylococcal infections. In three, cases 16, 17 and 18, the infection was with Strept. viridans but there was no cardiac lesion or systemic emboli to suggest subacute bacterial endocarditis.

In case 19, a bloodstream infection with a β haemolytic Streptococcus occurred in a man who had received radiotherapy in 1944 for epithelioma of the penis and again in 1952 and 1954 for carcinoma of the palate with secondary deposits in cervical glands. On admission, anaemia (Hb. 10.4 g. per cent.) and leucopenia (polymorphs 3,629 per cm.) were present.

Case 20 had had a course of radiotherapy in 1947, after a diagnosis of lymphosarcoma had been made. On admission, she was anaemic (Hb. 9.7 g. per cent.) but there was a polymorphonuclear leucocytosis (85.5 per cent. of a total count of 11,400 per cm.). Four days before admission, she had coughed up a large quantity of purulent sputum, suggesting spontaneous drainage of a lung abscess. A blood stream infection with pneumococci was present on admission to hospital, supporting this diagnosis, although no abscess was seen on chest X-ray.

Only in Case 21 was shock a serious therapeutic problem. Meningococcal septicaemia with meningitis was diagnosed in this 27-year-old Arab. Thirty-six hours after the onset of this illness, hypotension occurred, which could only be overcome by intravenous noradrenaline and hydrocortisone. This treatment had to be continued for a week and appeared to be life-saving. His convalescence was stormy and included a psychotic episode, but his only residual disability was deafness.

Case 22 was a woman suffering from rheumatoid arthritis who had had one adrenal gland removed for inoperable breast carcinoma. Blood was transfused in preparation for the second stage adrenalectomy. Fever and jaundice developed and B. coli and Staph. albus were both isolated from two blood cultures. It is unlikely that the donor blood was infected, as the acute illness and profound shock seen in cases transfused with infected blood did not occur.

Case 23 was admitted as an acute abdominal emergency. At laparotomy, there was early peritonitis for which no primary cause was found. Blood culture and culture of a peritoneal swab taken at operation both yielded a growth of B. anitratum. Post-operatively, there was an episode of hypotension successfully treated by methidrine and intravenous fluids.

Case 24 was a Pakistani, who had been in England three weeks, and had an infection with Salmonella paratyphi A. This responded to a course of chloramphenicol.

Discussion

Nineteen of the 24 patients were male and five were female. Thirteen of the cases were in the fifth and sixth decades.

The probable source of infection was known in 9 cases (Table 1). Of these, two had chronic osteomyelitis, which is noteworthy as this disease is becoming less common. In four cases, operations preceded infection. Minor surgical procedures were apparently responsible in three cases. Only once was an intravenous drip incriminated, though Spink (1956) and Collins et al. (1956) have stressed the number of cases of staphylococcal septicaemia apparently due to the spread of in-
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Race</th>
<th>Significant Pre-existing Disease</th>
<th>Source of Infection</th>
<th>Previous Cortisone Therapy</th>
<th>Operation or Injury</th>
<th>Organism from Blood Culture</th>
<th>Sensitivity</th>
<th>Antibiotics Used</th>
<th>Outcome</th>
<th>No. of Days to Death or Discharge</th>
<th>Cause of Death</th>
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<td>Drainage of prostatic abscess</td>
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<td>R (S) S R R (S)</td>
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<td>Staph. aureus coagulase + B. coli</td>
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<td>—</td>
<td>B. friedlander</td>
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<td>—</td>
<td>—</td>
<td>S S S S S</td>
<td>P T</td>
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<td>R (S) (S) (S)</td>
<td>P T St</td>
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<td>16</td>
<td>M</td>
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<td>(S) (S) (S)</td>
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<td>Strept. viridans</td>
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<td>—</td>
<td>B-Haemolytic Strept. pyogenes</td>
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<td>—</td>
<td>Pneumococcus</td>
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<td>Arab</td>
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<td>S S S S S</td>
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<td>A</td>
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<td>—</td>
<td>B. anitratum</td>
<td>R R S S</td>
<td>P T</td>
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<td>Bronchiectasis</td>
<td>—</td>
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<td>—</td>
<td>S. paratyphi A.</td>
<td>R R S S</td>
<td>R P C</td>
<td>A</td>
<td>6— transfer</td>
<td>—</td>
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Abbreviations:  
P = Penicillin  
R = Resistant  
S = Fully sensitive  
(S) = Partially sensitive  
C = Chloramphenicol  
T = Tetracycline  
E = Erythromycin  
A = Alive  
D = Dead  

One patient (case 16) was receiving cortisone treatment for chronic disease (systemic lupus erythematosus). Similar cases have been reported (Spink, 1956; Shaper and Dyson, 1955). Two patients had had radiotherapy some years before the onset of the acute illness. Kaplan et al. (1952) and Bond et al. (1952) have found a transient increase in the incidence of infection in experimental animals following X-irradiation.

The association of fatal septicaemia with liver disease is recognised (Martin et al., 1956). These authors suggest that there may be a defect in the immunological defences of the body or a portal-systemic bypass. The latter would seem to be a reasonable explanation if the source of infection were within the area drained by the portal vein. In the present series, evidence of liver disease was found in ten cases (Table 2). In cases 6, 8, 9, 10 and probably 21, this was present before the bloodstream infection occurred. Cases 1, 5, 7, 19 and 22 had no obvious evidence of pre-existing liver disease. Jaundice developed terminally in case 1. In case 5, liver function tests were initially normal. Later, deep jaundice appeared and the mode of death suggested liver failure, but liver function tests were not repeated at this stage. Histologically the liver showed centrilobular necrosis. Case 7 had jaundice, hypoalbuminaemia and multiple liver abscesses. The abnormal flocculation tests in case 19 can be explained by the high level of y-globulin. In case 22, jaundice, which may have been partly haemolytic was seen. Here again the y-globulin level was raised, a recognised finding in rheumatoid arthritis of long standing.

Profound hypotension was seen in three cases. Shock has frequently been observed in septicaemia (Braude et al., 1953; Altemeier and Cole, 1956). Hall and Gold (1952) noted the presence of shock in 35 of 100 patients with bacteraemia, 66 per cent. of whom were infected by Gram negative organisms. In five cases, there was a double infection. In the present series, two organisms were isolated from the blood in three cases, none of whom developed shock, and in only one of the three cases in whom shock occurred was the infecting organism Gram negative.

In three of the fatal cases (1, 3 and 5), acute staphylococcal endocarditis was found at autopsy on valves showing no evidence of previous rheumatic disease. Case 12 was a late death from acute staphylococcal endocarditis superimposed on pre-existing rheumatic heart disease. No clinical evidence of acute bacterial endocarditis was found in the three cases of staphylococcal septicaemia who recovered. Spink (1956) found a death rate of 94 per cent. in cases of staphylococcal septicaemia complicated by endocarditis.

Antibiotic treatment in septicaemia presents several problems. The patient may be too ill to wait for the results of blood cultures and antibiotic sensitivity tests. The onset of blood stream infection may be masked either by the presence of another disease, when the occurrence of deterioration in the patient's condition may not suggest septicaemia, or by treatment with corticoids, when the normal indications of infection may be absent. Prophylactic antibiotics may already have been given in surgical cases, or the septicaemia may arise late in the course of an infection already treated by antibiotics. Sometimes the response to antibiotic treatment may not correspond with the results of in vitro sensitivity tests.

As will be seen from Table 2, several antibiotics were given in most cases and in all the staphylococcal infections. One only, usually penicillin, was used when it was possible to wait for the identification of the organism and the results of sensitivity tests before starting treatment. In cases 1 and 5, the correct treatment was not started until just before death. Both these patients had fulminating infections with resistant
organisms which were insensitive to the antibiotics initially used in treatment.

**Conclusions**

The most important factor in deciding the outcome in this series of cases has been the type of infecting organism. Staphylococcus aureus was isolated from the blood in seven of ten fatal cases, one of whom (Case 4) was also infected by B.coli, and from the patient (Case 12) with acute bacterial endocarditis who died later. All four patients in whom death occurred in the absence of previous disease had staphylococcal septicaemia. The organism in three fatal cases was fully sensitive to antibiotics, whereas resistant, though presumably less virulent, staphylococci were isolated from the three survivors in the staphylococcal group.

Another important factor is pre-existing disease, which was present in this series in eight of the fatal cases and seven of those who recovered. Liver disease and malignant disease each accounted for five cases.

**Summary**

Twenty-four cases of septicaemia treated in a general hospital in 15 months are described. Of these 12 died.

The series included 11 cases of infections with Staphylococcus aureus of whom eight died.

Pre-existing disease was apparently an aetiological factor in 15 cases. Eight of these died.

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Septicaemia in a General Hospital

Mary Bateman and W. A. Hudson

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